DETAILED ACTION

Election/Restrictions

Claims 40-47 provide for the use of a blocker of a protease inhibitor for the preparation for enhancing the effect of anti-cancer therapy, but, since the claims do not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to claim. Given that these claims may have dual interpretation either as a method of preparation or as a method of treatment, these claims are being interpreted herein as optionally both a method of making and a method of treating.

This application contains the following inventions or groups of inventions, which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

I. Group I, claims 1-18, 40-48, and 51-56 are drawn to a method for improving the effect of an anti-cancer therapy in a patient, the method comprising increasing the susceptibility of malignant cells in the patient to said anti-cancer therapy without substantially increasing the susceptibility of non-malignant cells to said anti-cancer therapy.

II. Group II, claims 19-29, 49-50, and 57 are drawn to a method for predicting whether a cancer patient will benefit from an anti-cancer therapy, where the efficiency of

said anti-cancer therapy depends on tumor tissue expression of protease inhibitors, the method comprising determining whether cells from tumor tissue in the patient expresses any one of a number of preselected protease inhibitors, and establishing that the patient will not benefit from the anti-cancer therapy if any one of said protease inhibitors is expressed beyond a relevant threshold value and establishing that the patient will benefit from the anti-cancer therapy if none of the preselected protease inhibitors are expressed beyond their relevant threshold values.

III. Group III, claims 30-36 are drawn to a method for identifying an agent that blocks the anti-apoptotic effect of a protease inhibitor, the method comprising providing a first population of malignancy-derived cells that are +/+ or +/- for said protease inhibitor or where the protease inhibitor is provided from an external source, providing a second population of malignancy-derived cells that are -/- for said protease inhibitor, subjecting samples of said first and second populations of cells to substantially the same apoptosis-inducing conditions in the absence and presence of a defined concentration of a candidate agent, determining the degree of apoptosis induced in said samples, and identifying the candidate agent as an agent that blocks the anti-apoptotic effect of the protease inhibitor if 1) the degree of apoptosis induced in the samples from the first population of cells is significantly higher in the presence of the candidate agent, and 2) the degree of apoptosis induced in the samples from the second population of cells is not significantly higher in the presence of the candidate agent.

IV. Group IV, claim 37 is drawn to a method for identifying an agent that blocks the anti-apoptotic effect of a protease inhibitor, the method comprising providing a first population of malignancy-derived cells that are +/+ or +/- for said protease inhibitor or where the protease inhibitor is provided from an external source, implanting the first population of cells in an experimental animal and allowing them to grow, subjecting the animal to apoptosis-inducing conditions in the absence and presence of a defined concentration of a candidate agent, determining the degree of tumor development and/or progression in said animal, determining the degree of apoptosis-related adverse effects in the animal, and identifying the candidate agent as an agent that blocks the anti-apoptotic effect of the protease inhibitor if 1) the degree of tumor development is significantly lower in the presence of the candidate agent, and 2) the degree of apoptosis-related adverse effects induced is not significantly higher in the presence of the candidate agent.

V. Group V, claim 38 is drawn to a method for identifying an anti-cancer treatment the efficacy of which is dependent on presence or absence of apoptosis-inhibiting protease inhibitors, the method comprising providing a first population of malignancy-derived cells that are +/+ or +/- for said protease inhibitor, providing a second population of malignancy-derived cells that are -/- for said protease inhibitor, subjecting samples of said first and second populations of cells to substantially the same anti-cancer treatment in the absence and presence of an effective concentration of an agent which blocks the apoptosis protecting effects of the protease inhibitor,

determining the degree of apoptosis induced in said samples, and identifying the anti-cancer treatment as one, the efficacy of which is dependent on presence or absence of apoptosis-inhibiting protease inhibitor if 1) the degree of apoptosis induced in the samples from the first population of cells is significantly higher in the presence of the agent, and 2) the degree of apoptosis induced in the samples from the second population of cells is not significantly higher in the presence of the agent.

VI. Group VI, claim 39 is drawn to a method for identifying an anti-cancer treatment the efficacy of which is not dependent on presence or absence of apoptosis-inhibiting protease inhibitors, the method comprising providing a first population of malignancy-derived cells that are +/+ or +/- for said protease inhibitor, providing a second population of malignancy-derived cells that are -/- for said protease inhibitor, subjecting samples of said first and second populations of cells to substantially the same anti-cancer treatment in the absence and presence of an effective concentration of an agent which blocks the apoptosis protecting effects of the protease inhibitor, determining the degree of apoptosis induced in said samples, and identifying the anti-cancer treatment as one, the efficacy of which is not dependent on presence or absence of apoptosis-inhibiting protease inhibitor if 1) the degree of apoptosis induced in the samples from the first population of cells is not significantly higher in the presence of the agent, and 2) the degree of apoptosis induced in the samples from the second population of cells is not significantly higher in the presence of the agent.

The inventions listed as Groups I, II, III, IV, V, and VI do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features.

An international application should relate to only one invention or, if there is more than one invention, the inclusion of those inventions in one international application is only permitted if all inventions are so linked as to form a single general inventive concept (PCT Rule 13.1). With respect to a group of inventions claimed in an international application, unity of invention exists only when there is a technical relationship among the claimed inventions involving one or more of the same or corresponding special technical features.

The expression "special technical features" is defined in PCT Rule 13.2 as meaning those technical features that define a contribution which each of the inventions, considered as a whole, makes over the prior art. The determination is made on the contents of the claims as interpreted in light of the description and drawings. Whether or not any specific technical feature makes a "contribution" over the prior art, and therefore constitutes a "special technical feature", should be considered with respect to novelty and inventive step.

In this instant application, there is no common technical feature in the aforementioned groups. Specifically, the Examiner contends that group I is directed to a method for improving the effect of an anti-cancer therapy in a patient comprising increasing the susceptibility of malignant cells to said anti-cancer therapy while

minimizing the susceptibility of non-malignant cells and does not necessarily involve the use of protease inhibitors. Group II, however is directed to a method of predicting whether a cancer patient will benefit from an anti-cancer therapy based on tumor tissue expression of protease inhibitors. Group III is directed to a method for identifying an agent that blocks the anti-apoptotic effect of a protease inhibitor by providing malignant cells and determining the degree of apoptosis induced in said cells *in vitro*. Group IV is directed to a method of identifying an agent that blocks the anti-apoptotic effect of a protease inhibitor, the method comprising testing said method *in vivo* based on protease inhibitors. Group V is directed to a method of identifying an anti-cancer therapy based on protease inhibitors. Group VI, on the other hand, is a method of identifying an anti-cancer therapy wherein said method does not depend on protease inhibitors. As a result, the Examiner maintains that these groups cannot be said to contain a common special technical feature.

Thus, no special technical features exist among the different groups because the inventions in Groups I, II, III, IV, V and VI fail to make a contribution over the prior art with respect to novelty and inventive step. In conclusion, there is a lack of unity of inventions, and therefore restriction for examination purposes as indicated is proper.

Species Election

This application contains claims directed to more than one species of the generic invention. Specifically, this application recites the use of blockers that possess

contrasting functions or mechanism of action (for example, polyclonal antibody vs. soluble receptor. Thus, these species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1.

The species listed below do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same special technical feature among the different species.

The species are as follows:

1) ***for Group I, II, III, IV, V, or VI***:

a) Applicant is required elect a particular protease inhibitor to be utilized in the aforementioned methods. Alternatively, applicant may elect a particular protease inhibitor listed in claims 4 or 48.

2) ***for Group I***:

a) Applicant is required elect a particular blocker to be utilized in the aforementioned method. Alternatively, applicant may elect a particular blocker listed in claim 5.

b) Applicant is required elect a particular anti-cancer therapy to be utilized in the aforementioned method. Alternatively, applicant may elect a particular anti-cancer therapy listed in claim 14.

c) Applicant is required elect a particular cancer to be targeted be utilized in the aforementioned method. Alternatively, applicant may elect a particular cancer to be targeted listed in claim 17.

Applicant is required, in reply to this action, to elect a single species to which the claims shall be restricted if no generic claim is finally held to be allowable. The reply must also identify the claims readable on the elected species, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered non-responsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

The following claims 1-57 are generic.

Applicant is also reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim

remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

No telephone call was made due to the complexity of the election/restriction.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Samira Jean-Louis whose telephone number is 571-270-3503. The examiner can normally be reached on 7:30-5 PM EST M-Th.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/S. J. L. /

Examiner, Art Unit 1627

03/18/10

/SREENI PADMANABHAN/

Supervisory Patent Examiner, Art Unit 1627